REMARKS/ARGUMENTS

Claims 1, 2, 4, 7, 8, 10 and 12-14 are pending in the application. No claims are allowed. Claim 1 has been amended. Claim 12 has been canceled. Entry of the amendment, reconsideration of the rejection, and allowance of claims 1, 2, 4, 7, 8, 10 and 12-14 are requested.

Applicants gratefully acknowledge the Examiner's withdrawal of the rejections under 35 U.S.C. § 112 and 102.

The Amendment

In order to expedite prosecution of the application and advance the case toward allowance, the claims have been amended. No new matter was introduced by this amendment.

Claim 1 has been amended to specify that the purified preparation of complete HAV particles has less than about 30 pg contaminating nucleic acid per IU HAV antigen. Support for this amendment can be found in the specification on page 9, paragraph [035]; page 14, paragraph [053]; and page 28, paragraph [105] as well as in original claim 12.

Rejection Under 35 U.S.C. §103

Claims 1-2, 4, 9-11 and 14 are still rejected under 35 U.S.C. §103(a) as being allegedly unpatentable over Robertson. *et al.* (USPN 5,268,292A), Provost *et al.* (USPN 4,783,407), Kistner *et al.* (WO 96/15231A2), Cinatl Jr. *et al.* (Biology International 1993, Vol. 17, No. 9, pp. 885-895) and Kuzuhara *et al.* (EP 0 339 667B1).

The Office Action reiterates that one would have been motivated by the cited references to generate the purified HAV particles by combining all well established methods in the art as described. The Office Action also asserts that the invention uses a diafiltration step (a combination of filtering plus dialyzing) and that Robertson *et al.* teach a final procedure of purification by using a Centriflo cone filter unit to filter and dialyze the isolated HAV particles and, thus, also use a diafiltration step. The Examiner concludes that the invention as a whole is *prima facie* obvious in the absence of unexpected results.

The rejection is respectfully traversed to the extent that the rejection applies to the claims as amended.

As was discussed in the last response, neither Robertson *et al.* nor Kuzuhara *et al.* teach a method of producing complete HAV particles in VERO cells. Robertson employs a fetal rhesus monkey kidney cell line (FRhK4 cells) (see column 8, line 65) and Kuzuhara employs GL-37 cells, derived from African Green monkey kidney cells (see page 4, line 41). Besides that, Robertson *et al.* teach three filtering steps in their procedure (see previous response and column 5, lines 40-50 and column 6, lines 17-27). Robertson's or Kuzuhara's disclosure coupled with the knowledge of deriving HAV in VERO cells from homogenized cell culture (see Provost *et al.*, column 4, lines 6-7) and/or the knowledge that influenza virus can be produced by utilizing vertebrate cells (see Kistner *et al.*, page 31, lines 17-18) and/or the knowledge of VERO cells on a PVF culture surface for the propagation of coxsackie virus B4, herpes simplex virus, measles virus, and polio virus (see Cinatl Jr. *et al.*, abstract and page 887, column 1) does not teach the skilled artisan to produce the claimed invention because there is simply no motivation to combine these references.

The Office Action also indicates that the invention as a whole is *prima facie* obvious in the absence of unexpected results. Yet, the instant invention achieves unusually pure virus product compared to prior art methods. The claims have been amended to specify that the purified preparation of complete HAV particles has less than about 30 pg contaminating nucleic acid per IU HAV antigen. In fact, the Applicants have shown that the filtering process is highly effective in reducing host cell contaminants. The grade of purity is increased by a factor of approximately 300, whereas the VERO cell DNA is reduced by a factor of approximately 9000 (see page 26 of the specification, paragraph [096]). In one of their examples, Applicants have achieved an antigen dose with less than 40 pg VERO cell nucleic acid per 100 IU HAV antigen which amounts to less than 8 pg DNA per 20 IU HAV antigen (see page 28 of the specification, paragraph [105]. Overall, the instant invention achieves a preparation of complete and pure HAV antigen that is substantially free of contaminating proteins and nucleic acids, wherein the

purity is greater than about 98% (see page 10 of the specification, paragraph [039]. None of the prior art references have disclosed such a pure virus product.

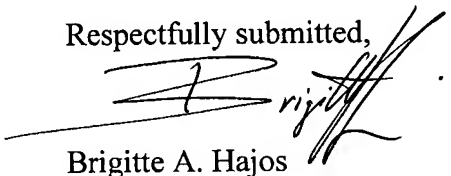
In light of the amendment an arguments presented above, Applicants respectfully request that the rejection of claims 1-2, 4, 9-11 and 14 under 35 U.S.C. §103(a), be withdrawn.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance and an action to that end is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 650-326-2400.

Respectfully submitted,



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Attachments
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